A platform for rapid generation of single and multiplexed reporters in human iPSC lines.

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Public Summary:
Induced pluripotent stem cells (iPSC) are important tools for drug discovery assays and toxicology screens. In this manuscript, we design high efficiency TALEN and ZFN to target two safe harbor sites on chromosome 13 and 19 in a widely available and well-characterized integration-free iPSC line. We show that these sites can be targeted in multiple iPSC lines to generate reporter systems while retaining pluripotent characteristics. We extend this concept to making lineage reporters using a C-terminal targeting strategy to endogenous genes that express in a lineage-specific fashion. Furthermore, we demonstrate that we can develop a master cell line strategy and then use a Cre-recombinase induced cassette exchange strategy to rapidly exchange reporter cassettes to develop new reporter lines in the same isogenic background at high efficiency. Equally important we show that this recombination strategy allows targeting at progenitor cell stages, further increasing the utility of the platform system. The results in concert provide a novel platform for rapidly developing custom single or dual reporter systems for screening assays.

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